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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/833,496	04/11/2001	Samuel H. Gellman	09820.149	4334

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EXAMINER	
GROSS, CHRISTOPHER M	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 01/10/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/833,496	GELLMAN ET AL.	
	Examiner	Art Unit	
	Christopher M. Gross	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *28 October 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-29* is/are pending in the application.

4a) Of the above claim(s) *3-5,9-11,15-23* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1,2,6-8,12-14 and 24-29* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *4/22/2002*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

1. Claims 1-29 are pending. Clams 3-5,9-11,15-23 are withdrawn. Claims 1,2,6-8,12-14 and 24-29 are examined herein.

Priority

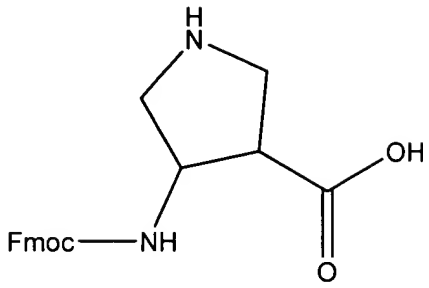
2. Applicant's claim for the benefit of a prior-filed application under 35 U.S.C. 119(e) or under 35 U.S.C. 120, 121, or 365(c) is acknowledged. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application). The disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

The disclosure of the prior-filed application, Application No. 60/039905, fails to provide adequate support or enablement in the manner provided by the first paragraph of 35 U.S.C. 112 for one or more claims of this application. The elected species is not disclosed in the provisional application.

Election/Restrictions

3. Applicant's election with traverse of a heterocyclic ring having one or more nitrogen atoms as the elected genus and Fmoc-4-aminopyrrolidine-3-carboxylic acid:



as the elected species in the reply filed on 10/28/2005 is acknowledged. The traversal is on the ground(s) that the species are not distinct and that the examiner has not provided sufficient scientific rationale that the species are indeed independent inventions. This is not found persuasive because the extensive ring substitutions listed in claim 1 will drastically change the beta amino acid both physically and chemically. For example an alkylsulfonyl substitution, representing an additional charge as well as being a good leaving group, will change the solubility characteristics and reactivity profile of the beta amino acid. Furthermore, biological activity will vary considerably amongst the members of the improper Markush group, as illustrated by Nagase et al wherein the seemingly minor change of swapping a hydrogen atom for fluorine reversed the activity of an opioid receptor pharmacophore from an antagonist into an agonist (Nagase et al 2001 Life Sciences 68:2227-2231). Each of these criteria lends credence to the fact that the various claimed beta amino acids in claim 1 lack a structural or functional core.

The requirement is still deemed proper and is therefore made FINAL.

Claims 3-5,9-11,15-23 are withdrawn from further consideration pursuant to 37 CFR 1.142(b), as being drawn to a nonelected species, there being no allowable generic or linking claim. Applicant timely traversed the restriction (election) requirement in the reply filed on 8/25/2005.

Claim Rejections - 35 USC § 112, First Paragraph

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

4. Claims 1,2,6-8,12-14 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for acid labile primary amino protecting groups, does not reasonably provide enablement for base labile primary amino protecting groups, such as Fmoc in the elected species. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

There are many factors be considered when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether undue experiment is necessitated. These factors can include, but are not limited to:

(1) the breadth of the claims;
(2) the nature of the invention;
(3) the state of the prior art;
(4) the relative skill of those in the art;
(5) the level of predictability in the art;
(6) the amount of direction provided by the inventor;
(7) the existence of working examples; and
(8) the quantity of experimentation needed to make or use the invention based on the content of the disclosure.

In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988).

(1 and 2) The breadth of the claims and the nature of the invention: The claimed invention is drawn to a broad range of beta amino acids, lacking a structural or functional core. The elected species is Fmoc-4-aminopyrrolidine-3-carboxylic acid (see structure above).

(3 and 5) The state of the prior art and the level of predictability in the art:

During solid-phase peptide synthesis - the intended use of the beta amino acids reflected in the specification on page 55 - the "temporary" N-terminal protecting group Fmoc (Grant, 1992 Synthetic Peptides – A Users Guide p 84) is removed under alkaline conditions, typically with secondary amines like piperidine. Premature removal of the temporary protecting group, however, such as promoted by the secondary amine located on pyrrolidine ring of the elected species itself, will lead to extra amino acid insertions, incomplete couplings and other side reactions. Furthermore, the lack of a protecting group on the secondary amine of Fmoc-4-aminopyrrolidine-3-carboxylic acid will lead to branched peptide formation. Thus, attempting peptide synthesis with the elected species will result in an intractable mixture of products.

(4) The level of one or ordinary skill: The level of skill would be high, most likely at the Ph.D. level or equivalent number of years experience. However, such persons of ordinary skill in this art, *given its unpredictability*, would have to engage in undue (non-routine) experimentation to carry out the invention as claimed.

(6 and 7) The amount of direction provided by the inventor and the existence of working examples: Applicant teaches protection of the secondary nitrogens on pages

23,25 and 29 of the specification and reaction 5c of the amendment dated 4/11/2001, however the elected species is not adequately protected for the intended use of peptide synthesis. The specification does not present a protocol to prevent the self-mediated premature deprotection of Fmoc-4-aminopyrrolidine-3-carboxylic acid, described above.

(8) The quantity of experimentation needed to make or use the invention based on the content of the disclosure: As the elected species is difficult to work with, the amount of additional experimentation necessary is substantial. One of skill in the art would not be able to use the invention to consistently prepare peptides due to the multitude of side reactions that would occur (see above). One of skill in the art would not be able to make the invention since the elected species would decompose. Other species of the elected genus comprising secondary amines similarly lack enablement if not appropriately protected. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make and use the invention as claimed.

5. Claims 1,2,6-8,12-14 and 24-29 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter, which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventors), at the time the application was filed, had possession of the claimed invention. This is lack of written description rejection.

The claimed invention is drawn to a broad range of beta amino acids, lacking a structural or functional core. The elected species is Fmoc-4-aminopyrrolidine-3-carboxylic acid (see structure above).

Vas-Cath Inc. v. Mahurkar, 19USPQ2d 1111, clearly states that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116).

The skilled artisan cannot envision using the elected species for the intended use of peptide synthesis. Conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the technique.

Therefore, only adequately protected beta amino acids, such as compound 58 on page 29 of the specification, but not the full breadth of the claims meets the written description provision of 35 U.S.C. §112, first paragraph. Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 U.S.C. §112 is severable from its enablement provision (see page 1115).

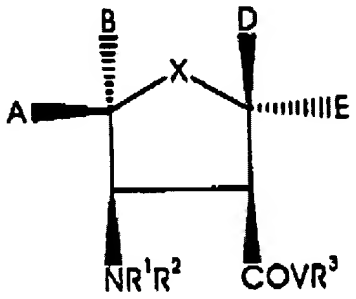
Claim Rejections - 35 USC § 102

(b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

6. Claims 1,2,6-8,12-14 and 24-29 are rejected under 35 U.S.C. 102(b) as being anticipated by Crowley, et al (WIPO 95/07022).

The claimed invention is drawn to beta amino acids, the elected genus comprising a heterocyclic ring having one or more nitrogen atoms and Fmoc-4-aminopyrrolidine-3-carboxylic acid is the elected species (see structure above).

Crowley, et al throughout the publication and especially page 1 and the abstract, disclose the following structure:



wherein A,B,D,E, and R^3 are hydrogen, V is oxygen, X is NR^8, R^2 or R^1 is an amine protecting group or hydrogen or vice versa, and R^8 is hydrogen which reads on the elected species.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. A nonstatutory obviousness-type double patenting rejection is appropriate where the conflicting claims are not identical, but at least one examined application claim is not patentably distinct from the reference claim(s) because the examined application claim is either anticipated by, or would have been obvious over, the reference claim(s). See, e.g., In re Berg, 140 F.3d 1428, 46 USPQ2d 1226 (Fed. Cir. 1998); In re Goodman, 11 F.3d 1046, 29

USPQ2d 2010 (Fed. Cir. 1993); In re Longi, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); In re Van Ornum, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); In re Vogel, 422 F.2d 438, 164 USPQ 619 (CCPA 1970); and In re Thorington, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) or 1.321(d) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent either is shown to be commonly owned with this application, or claims an invention made as a result of activities undertaken within the scope of a joint research agreement.

7. Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).Claims 1,2,6-8,12-14 and 24-29, drawn to beta amino acids are provisionally rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 4-6,8,9, drawn to peptide "foldamers," of copending Application No. 10/648089. Although the conflicting claims are not identical, they are not patentably distinct from each other because one of skill in the art would anticipate the genus of beta amino acids in the instant application based on the peptide species of disclosed in applicaton 10/648089.

This is a provisional obviousness-type double patenting rejection because the conflicting claims have not in fact been patented.

8. Claims1,2,6-8,12-14 and 24-29, drawn to beta amino acids are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1 and 2, drawn to a combinatorial peptide library comprising beta amino acids of U.S. Patent No. 6613876. Although the conflicting claims are not identical, they are not patentably distinct from each other because one of skill in the art would anticipate the

genus of beta amino acids in the instant application based on the peptide library species of disclosed in US patent 6613876.

9. Claims1,2,6-8,12-14 and 24-29, drawn to beta amino acids are rejected on the ground of nonstatutory obviousness-type double patenting as being unpatentable over claims 1-6,11-20 drawn to peptides comprising beta amino acids of U.S. Patent No. 6060585. Although the conflicting claims are not identical, they are not patentably distinct from each other because one of skill in the art would anticipate the genus of beta amino acids in the instant application based on the peptide species of disclosed in US patent 6060585.

Conclusion

10. Claims 1,2,6-8,12-14 and 24-29 are not allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christopher M. Gross whose telephone number is (571)272-4446. The examiner can normally be reached on M-F 9-5:30.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Andrew Wang can be reached on (571)272-0811. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR.

Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Christopher M Gross
Examiner
Art Unit 1639

cg

Mark Shibuya
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